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The polygenic risk for cannabis initiation and cannabis use disorder in individuals with cannabis and multiple drug use disorders and comorbid psychiatric disorders

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The prevalence of life-time SUD among people having a major psychiatric disorder is ~30% in Denmark. Genome-wide association studies (GWASs) have shown that the high comorbidity to some extent can be explained by shared common risk variants. For cannabis, recent studies suggest that initiation has a different underlying genetic architecture than cannabis use disorder (CUD). However, little is known about the potential differences in the polygenic risk load of cannabis initiation and CUD among comorbid psychiatric disorders in individuals with SUD.

We will report results from polygenic risk score (PRS) analyses of cannabis initiation and CUD in 7,000 individuals with CUD, 4,000 individuals with multiple drug use disorder (MUD) and 40,000 controls from the iPSYCH cohort. Since we can access all diagnoses in the registers for the included individuals, we will perform detailed PRS analyses in CUD and MUD stratified by comorbid psychiatric disorders. The PRSs will be trained on the large GWAS meta-analysis of cannabis initiation and our new CUD GWAS meta-analysis. In order to compare mean PRS between the comorbid groups the normalized PRS scores will be regressed on the subgroups in a multivariate regression.

The results will elucidate if the polygenic risk load for cannabis initiation and CUD differ among comorbid psychiatric disorders in individuals with CUD and MUD, and further more elucidate if the more severe phenotype, MUD, has a higher polygenic risk load. The results will increase our understanding of the genetic architecture underlying CUD and how it differs among comorbid psychiatric disorders.